REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

As noted in the Office Action Summary, claims 1-16 and 19-26 are currently pending. Claims 1, 2, 6 and 22 are amended herein to recite that the claimed monoclonal antibodies can monitor the activity of systems involving serpin protein C inhibitors. Support for this amendment may be found throughout the specification and claims as-filed, especially at page 2, lines 29-37; page 3, lines 7-12.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-16, 19-26 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a protein C inhibitor (PCI), purportedly fails to provide enablement for any inhibitor.

In the interest of expediting prosecution, and without acquiescing in the rejection, the claims are amended herein to recite that the inhibitors of the claimed methods are serine proteinase inhibitors of the serpin super family. Specifically, claim 1 is now directed to a monoclonal antibody suitable for monitoring the activity of systems involving the serpin protein C inhibitor, said monoclonal antibody having specific affinity for both a complex between a serine proteinase and a serine proteinase inhibitor of the serpin group, and a cleaved an uncomplexed form of said serine proteinase inhibitor of the serpin group, while having no specific affinity for said inhibitor in its uncleaved and active form of said serine proteinase inhibitor of the serpin group. The claimed antibody is selective in relation to serine proteinase

inhibitors of the serpin group, and thus supported by the specification such that the skilled artisan could make and/or use the present invention.

Serine proteinase inhibitors of the serpin group are well supported in the specification. Working examples directed to serpins may be found in the specification as well. Applicant refers to pages 13-19, disclosing the purification of the serpins, production of appropriate monoclonal antibodies and their characterization, and the assaying of blood samples. In addition, Applicant notes that page 17 of the present specification shows the considerable differences is present between the complexed on one side and non-complexed, cleaved inhibitor on the other.

As stated in *Ex parte Forman* (230 USPQ 546 1986) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. In light of the amendments made herein, the claims as directed to serpin serine proteinase inhibitors and are well discussed in the specification. The claims would not require undue experimentation by the skilled artisan in order to practice the present invention.

The Office Action requests clarification between the structure and function of the antibody of the present invention. To this end, Applicant submits that the inhibitor is cleaved in the active site loop, and that this cleavage makes the loop turn in through the structure of the inhibitor and open up for a site where the antibody can

bind. Applicant submits herewith three references in support of the structure and function of the molecules used in the present invention.

Enclosed is a copy of Suzuki et al., "Characterization of a cDNA for Human Protein C Inhibitor", *Journal of Biological Chemistry*, 262:611-616 (1987). Suzuki discloses the cloning of PCU cDNA comprising a several sequenes for other serpins as well, such as antithrombin and antitrypsin.

By way of explanation and further support, Applicant again refers to Gettins, "Serpin Structure, Mechanism, and Function", *Chemical Reviews* 102:4751-4803 (2002) (copy also enclosed). Gettins provides a detailed review of the serpin super-family and its clades, including proteinase inhibitors. Pages 4754 and 4757 and 17 discuss functions of human serpins, for example. Page 4672 discloses conformational changes as the serpin molecule folds. Serpin inhibition of proteinases is also discussed, for example, at pages 4764 to the end. Antithrombins are discussed at page 4785.

Huntington et al. "Crystal Structure of Protein C Inhibitor Provides Insight into Hormone Binding and Heparin Activiation", Structure 11:202-215 (2003), is also provided for purposes of explanation. Huntington provides an explanation of the functionality of protein C inhibitors, as members of the serpin family.

Finally, as set forth in the previous Response, Applicant has provided support for antibodies against antitrombin, which is another serine proteinase inhibitor, very similar to protein C inhibitor, and thus provides further evidence of the functionality of the present invention.

Claims 1-16, and 19-26 stand rejected under 35 U.S.C. § 112, first paragraph, for purportedly failing to comply with the written description requirement.

Specifically, the Office Action states that the claims are drawn to a monoclonal antibody having specificity for both (1) complex between serine proteinase and inhibitor thereof; and (2) a cleaved an uncomplexed form of said inhibitor, while having no specific affinity for said inhibitor in its uncleaved and uncomplexed form. As indicated on the bottom of page 2 of the Office Action, the Office Action appear to state that as claim 1 recites a complex "between a serine proteinase and an inhibitor thereof", that Applicant is claiming an inhibitor of serine proteinase.

However, by way of clarification, Applicant submits that the present invention is directed to a monoclonal antibody suitable for the registration of the activity in a system comprising protein C inhibitors of the serpin group, whereby the antibody has specific affinity for both a complex between a serine proteinase and a serine proteinase inhibitor of the serpin group, and a cleaved and uncomplexed bound form of said serine proteinase inhibitor of the serpin group. The antibody does not have any specific affinity for the uncleaved and active form of said serine proteinase inhibitor of the serpin group. Therefore, the antibody is selective in relation to serine proteinase inhibitors of the serpin group.

In light of the above, Applicant requests that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-16 and 19-26 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite. Regarding claim 1, step (i), the Office Action states that the phrase "an inhibitor thereof" is indefinite, as it is purportedly unclear whether this inhibitor relates to the "protein C inhibitor", or to the complex. Claim 1 is

amended herein to remove the phrase "inhibitor thereof". Thus, this rejection is moot.

Regarding claim 1, step (ii), the Office Action states that the phrase "a cleaved an uncomplexed form " is indefinite, and suggests that claims 1 and 2 be amended to recite "a cleaved and uncomplexed form". As amended herein, claim1 or 2 no longer recites this phrase and thus the rejection is moot.

Regarding claim 1, line 9, the Office Action states that the phrase "a derivative" is indefinite, because it is purportedly unclear as to what is the "derivative" in the context, *e.g.*, chemical modification, or recombinant substitution. Claim 1 is amended herein to remove the term "derivative" and thus this rejection is moot.

Regarding claim 1, line 2, the Office Action states that the phrase "the same biological activity" is indefinite, because it is purportedly not clear what biological function is referred to, *e.g.*, binding affinity, serine proteinase inhibitor, or protein C inhibitor. Claim 1 is amended herein, and no longer recites "same biological activity". Thus, this rejection is moot.

In light of the above amendments and remarks, Applicant respectfully requests that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

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By: _____
Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

VA 435707.1